respectfully requested that this rejection is improper and should be withdrawn. It is believed that all pending claims are in condition for allowance, an early notice of which is earnestly solicited.

I. The Disclosed Invention

The present application, entitled "Pharmaceutical Compositions", relates to (i) methods of treatment of a variety of disorders using nedocromil acid or pharmaceutically acceptable salts thereof, such as nedocromil sodium as the active ingredient, which is administered in aqueous solution and to (ii) novel pharmaceutical compositions for use in such methods. Four varieties of disorders are described in the application as being treatable with the methods and compositions of the invention, including (1) six types of eye conditions; (2) three types of nasal conditions; (3) reversible obstructive airways disease; and (4) and three types of colon conditions. The aqueous solution is administered by a route appropriate to the condition being treated. Thus, for treatment of eye conditions, administration may be to the eye itself; for treatment of nasal conditions, intra-nasally with a nasal spray; for reversible obstructive airway disease, by inhalation as a nebulised cloud; and, for treatment of colon conditions, rectally as an enema.

II. The Recapture Estoppel Doctrine Does Not Apply To Reissue Application Claims 1-3

The final rejection alleges that reissue application claims 1-3 are an improper recapture of broadened subject matter. This rejection is legally incorrect. Reissue claims 1-3 are identical to claims 1-3 of the '833 patent. Thus, they were not finally rejected during the original

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reissue application claim 4 was cancelled in a reply mailed on July 9, 2001, in response to an Office Action dated April 13, 2001. Thus, it appears that the rejection is directed to only claims 1-3 and 10-19. This is consistent with the claims identified as being rejected in box 6 of the Office Action Summary.

prosecution; they were allowed. These claims were not broadened claimed subject matter surrendered in the original prosecution. They claim subject matter identical to the claimed subject matter that was allowed during the original prosecution. For the above reasons, the rejection of claims 1-3 is improper and should be withdrawn.

III. The Final Rejection Incorrectly Refers to Reissue Application Claims 4-13

The Office Action dated 6/28/02 states that the "instant reissue application contains the same three claims [i.e., reissue application claims 1-3 are identical to claims 1-3 of the '833 patent] as well as Claims 4-13." (Office Action at 2). The Office Action continues, "Claims 4-13 were present in the prosecution of the original application but were cancelled after a final rejection filed February 13, 1995." (Office Action at 2-3). These statements, however, do not appear to correctly reflect the status of the claims in the record in this case. It appears that the reference to claims 4-13 was intended to refer to (i) the pending reissue application method of treatment claims, originally filed in the reissue application as new claims 4-9, and that have been renumbered to claims 14-19; and (ii) the pending method of controlling claims 10-13. With this understanding, reference will hereinafter be made to the pending method of treatment claims 14-19 and the pending method of controlling claims 10-13.

IV. The Recapture Estoppel Doctrine Does Not Apply To Reissue Application Claims 14-19

Reissue application method of treatment claims 14-19 are directed to treatment of 4 types of eye diseases using the active ingredient of the present invention. The recapture estoppel doctrine does not apply to these claims for the reasons that these claims qualify under two exceptions to the recapture estoppel rule. First, this subject matter was not surrendered during

the original prosecution of the application because there is no admission that the patentee considered the subject matter to be, in fact, not patentable. Second these claims are materially narrower than any abandoned claim in regard to an aspect that was overlooked during the original prosecution.

A. There is no admission that the patentee considered the subject matter of reissue claim 14 to have been, in fact, not patentable during the original prosecution

It is well settled that one aspect of applying the recapture estoppel doctrine is ". . . to determine whether the broader aspects of the reissued claim relate to surrendered subject matter." *In re Clement*, 131 F.3d 1464, 1468-9, 45 USPQ2d 1161, 1163 (Fed. Cir. 1997). However, it is also well settled that an exception to application of the rule exists when there is no admission by the patentee that the relevant subject matter is, in fact, not patentable. Not all subject matter that may have been claimed at one time during prosecution of the application but not found in the patent claim is "surrendered subject matter" for the purpose of the recapture estoppel doctrine. Specifically, the Federal Circuit has emphasized that ". . . the recapture rule does not apply in the absence of evidence that the applicant's amendment was 'an admission that the scope of that claim was not in fact patentable. [Emphasis added]'" *Id.* (quoting *Seattle Box. Co. v. Indus. Crating & Packing, Inc.*, 731 F2d 818, 826, 221 USPQ568, 574). In other words the absence of such an admission is an exception to application of the recapture rule. To determine whether this exception is present, one must ". . . look to the prosecution history for arguments and changes to the claims made in an effort to overcome a prior art rejection." *Clement, supra*, 131 F.3d at 1469, 45 USPQ2d at 1164, *citing Mentor,* 998 F.2d at 995-96, 27 USPQ2d at 1524-25; *Ball Corp. v. United States,* 729 F2d 1429, 1436, 221 USPQ 289, 294-95 (Fed. Cir. 1984).

It appears that in the final rejection the examiner is alleging that the method of treating the 4 eye diseases (conjunctivitis, keratitis, allergic eyes and anterior uvetis) of claim 14 was included in application claim 18, prosecuted in application Serial No. 08/082,804 and finally rejected in an Office Action dated October 19, 1994 (Paper 43)[2]. However, that application claim 18 became part of the application in a preliminary amendment dated August 7, 1991 (PTO Date Stamp) in application Serial No. 07/742,574. That claim 18 was directed to treatment of 6 eye diseases, including the 4 eye diseases of reissue application claim 14, as well as to 2 other eye diseases, to 3 types of nasal diseases, to reversible obstructive airways disease and to 3 types of colon diseases. This original prosecution claim 18 was never rejected on any ground related to eye disease prior art, and applicants never admitted the claimed treatment of any of the 6 eye diseases was, in fact not patentable. Rather, all of the prior art rejections to this claim 18 were made on the ground that certain prior art rendered unpatentable the generic claim because of prior art teachings directed to the "reversible obstructive airways disease."[3]

Although this application claim 18 was cancelled in favor of new claim 23, this amendment to the claims was done "in order to present the rejected claims in a better form for allowance or appeal." (Amendment "B" mailed February 13, 1995, at 2). Furthermore,

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2 The final rejection of June 28, 2002, appears to refer to a final rejection dated February 13, 1995. However, the record indicates that the Office Action dated February 13, 1995 refers to cancellation of claim 18, not to final rejection of claim 18. On February 13, 1995, Applicants mailed an amendment that included cancellation of application claim 18 that had been finally rejected on October 19, 1994, and replaced cancelled claim 18 with new claim 23. This new claim 23 was renumbered and issued as claim 1 of the '833 patent.

3 *See* Office Action mailed October 19, 1994 at 2-3 (rejections based on Brown, Cox and GB '291).

Applicants specifically denied that the remaining subject matter of claim 18 was, in fact, not patentable when they stated:

> This amendment was not presented earlier because Applicants believed, and still believe, that the claim amendments and reasoning set forth in Amendment "A", filed July 11, 1994, were sufficient to overcome the rejection under 35 U.S.C. §103 [to claim 18 that included treatment of the 6 eye diseases].

Amendment "B" mailed February 13, 1995, at 2-3.

Thus, as shown above, there is no evidence in the record that applicants admitted that the treatment of eye disease subject matter of reissue application claim 14 was not, in fact patentable. To the contrary, applicants expressly asserted that this subject matter was patentable.

For all of the reasons set forth above, reissue application claims 14-19 qualify as an exception to the recapture rule, and the rejection to these claims should be withdrawn for this reason alone.

B. Reissue application claims 14-19 qualify as a second exception to application of the recapture rule because they are materially narrower than finally rejected application claim 18 regarding overlooked, eye disease treatment subject matter

While in its broad form, the recapture estoppel doctrine prevents a patentee from regaining through reissue subject matter surrendered in an effort to obtain allowance of the patent claims, it is also well settled that a second exception to application of the rule exists when " . . .the reissued claims were materially narrowed in other respects to avoid the recapture rule." *Pannu v. Storz Instrument, Inc.*, 258 F.3d 1366, 59 USPQ2d 1597 (Fed. Cir. July 25, 2001), *citing Hester Indus., Inc. v. Stein, Inc.*, 142 F.3d 1472, 1482-83, 46 USPQ2d 1641 (Fed. Cir. 1998).

Application claim 18 was cancelled and replaced with new claim 23 on February 13, 1995, as referred to in the Office Action dated 6/28/02 (see footnote 2 above). However, the

exception to the recapture estoppel doctrine applies here because the original prosecution claim 18 broadly covered 6 types of eye diseases. In contrast, the broadest pending reissue application claim, claim 14, is limited to treatment of only 4 eye diseases. As will now be explained, this change in scope is clearly a material narrowing.

Reissue claim 14 is a two-part claim that includes a Markush genus of diseases that may be treated with the active ingredient of the present invention and a "normal format" method claim for particularly pointing out the method of administration of the active ingredient. A Markush claim is generally considered to be somewhat atypical, within the general context of claim formats.

Reissue application claim 14 is a Markush claim because it recites members of a group (the Markush group) in the form ". . . selected from the group consisting of A, B . . .." *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925). Also, reissue claim 14 is a generic claim because the claimed group is expressed as a group consisting of certain specified materials. Such claims are expressly sanctioned by the Manual Of Patent Examining Procedure ("MPEP"). *See, e.g., MPEP §§ 803.02, 2173.05(h), 2173.05(o)*. In this regard, it is improper to use the term "comprising" to introduce the group; the correct introductory term is "consisting of." *Ex parte Dotter*, 12 USPQ 382 (Bd. App. 1931).

The materials set forth in the Markush group ordinarily must belong to a recognized physical or chemical class or to an art-recognized class. However, when the Markush group is found in a claim reciting a process, it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is mainly responsible for their

function in the claimed relationship. *MPEP, supra, § 2173.05(i).* In regard to reissue application claim 14, the Markush group appears to include four types of eye diseases. These diseases are not only described in the specification, but also specific definitions for some of them are provided at [1:55-2:3][4]. These 4 types of eye diseases have in common their susceptibility to treatment with an aqueous solution of the active ingredient of the present invention.

Not only are Markush claims somewhat atypical in the manner by which a genus may be claimed, they are also somewhat atypical in the sense that changes in claim language often have a result in terms of claim scope that is opposite to the result of an identical change of claim language made to a typical, non-Markush claim. For example, in a typical, non-Markush claim, addition of claim terms ordinarily results in a narrowing of claim scope. However, because of the language used to define the genus in a Markush claim, the addition of terms, i.e., the addition of members to the group in a Markush group ordinarily results in a broadening of claim scope. Similarly, amendment of a "normal" claim through removal or deletion of a claim term usually results in a broadening of the scope of the claim. In contrast, amendment of a Markush claim through removal or deletion of one or more members of its Markush group usually results in a narrowing of the scope of the claim. This concept is important in the area of recapture estoppel because the outcome of particular tests used in application of the recapture estoppel doctrine often depends on whether a certain claim has been broadened or narrowed by amendment, and because the case law often refers to such broadening or narrowing only in terms of adding or deleting claim terms without mentioning the type of claim. In the absence of mentioning the

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4 Citation to the specification will be made to the specification as formatted in the '833

type of claim, it us usually assumed that a "normal" claim, rather than a "Markush" claim is at issue. Thus, in order to avoid drawing a wrong conclusion on the basis of wrongly evaluating claim scope changes, it is especially important to consider the specific nature of the Markush claim at issue here. In so doing, it is clear that application claim 14 (which addresses 4 types of eye diseases) is narrower than claim 18 (which addressed 6 types of eye diseases).

Also, as discussed above, it is readily apparent that the issue of patentability of the claims as related to treatment of eye disease prior art was overlooked during the original prosecution. The Patent Office made no prior art rejection to claim 18 that was grounded on eye disease prior art. As such, it is also readily apparent that this narrowing of claims scope was sufficient to qualify for the exception to the recapture rule.

In addition to the eye disease treatment aspects of the finally rejected claim 18 in comparison to reissue application claim 14, it is clear that claim 14 has been materially narrowed in several other aspects:

(1) Claim 18 broadly covers 3 types of nasal diseases, but reissue application claim 14 covers no nasal disease.

(2) Claim 18 broadly covers 3 types of colon diseases, but reissue application claim 14 covers no colon disease.

(3) Claim 18 broadly covers administering the active ingredient "to a patient," but reissue application claim 14 covers only administering the active ingredient "to the eye."

Thus, for all of the above reasons, reissue application claims 14-19 have been materially narrowed sufficient to escape the recapture estoppel rule, and the rejection should be withdrawn

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patent by column and line number. Thus [1:55 -2:3] refers to column 1, line 55 through column 2, line 3.

for this reason alone.

V. The Recapture Estoppel Doctrine Does Not Apply To Reissue Application Claims 10-13

As shown above, the recapture estoppel doctrine applies only to subject matter that has been surrendered during the original prosecution of the patent and does not qualify for an exception to the rule. In the Office Action dated 6/28/02, reissue application method of controlling claims 10-13 were also rejected under the recapture estoppel doctrine. However, no method of controlling claim was ever presented in the original prosecution. Thus, there was no surrender of such subject matter, and the recapture estoppel doctrine does not apply. For this reason the rejection to claims 10-13 should be withdrawn.

VI. Statement Under 37 C.F.R. 3.73

Pursuant to 37 C.F.R. 3.73(b), by and through its undersigned attorneys, such attorneys having the power to act on its behalf in this matter, Fisons plc hereby states that it is the assignee of all right, title and interest in United States Patent Number 5,443,833, and that it has the right to take action in this matter before the United States Patent and Trademark Office. Evidence of such ownership may be found in the records of the United States Patent and Trademark Office at Reel 4864, frame 113.

VII. Conclusion

For all the above reasons, it is believed that the rejections are improper and should be withdrawn. The claims of this application are believed to be in condition for allowance, an early notice of which is earnestly solicited. Applicants respectfully request that Examiner Joynes call Applicants' undersigned counsel should he have any questions concerning the above arguments

or wish to discuss any aspect of this application.[5]

Respectfully submitted,

Dated: September 25th, 2002

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5 To assist the Examiner in further consideration of this reissue application, see attached Table I which is a Summary of the Rejection, Amendment and Arguments from the original prosecution.

Table I

Table of Summary Rejections, Amendments and Arguments

Rejection No. & Date	Serial No. & Filing Date	Statutory Basis	Summary of Rejection	Summary of Responsive Claim Amendment & Date
1 7/20/88	'520 12/16/87	§112, ¶2	Claims 1-6 rejected as improper Markush group.	Amendment on 1/23/89 (PTO Stamp Date) replaced "comprising" with –consisting of – in claim 1. Claim 17 added.
2 7/20/88	'520 12/16/87	§102 (b), (e)	Claims 1-16 rejected as anticipated by Cairns and Dicker on treatment of asthma, colitis and reversible obstructive airways disease	In 1/23/89 amendment, the anticipation rejection was traversed by a showing of limitations in the rejected claims not found in single prior art reference.
3 7/20/88	'520 12/16/87	§102 (b)	Claims 1-16 rejected as anticipated by Cox on treatment of reversible obstructive airways disease	In 1/23/89 amendment, the anticipation rejection was traversed by a showing of limitations in the rejected claims not found in single prior art reference

4 4/3/89	'520 04/03/89	§102 (b), (e)	Claims 1-17 rejected as anticipated by Cairns and Dicker on ground that each anticipates treatment of asthma, colitis and reversible obstructive airways disease	Amendment of 6/29/89 submitted, but not entered into the application. Amendment argued that all claims require (1) aqueous solution and (2) specific active ingredient. No single reference (Cairns, Dicker or Cox) discloses both.
5 4/3/89	'520 04/03/89	§103	Claims 1-17 rejected as obvious over Cairns and Dicker on ground that they render treatment of asthma, colitis and reversible obstructive airways disease obvious	Amendment of 6/29/89 includes declaration of unexpected results submitted. Amendment not entered into the application.
6 4/3/89	'520 04/03/89	§102 (b)	Claims 1-17 rejected as anticipated by Cox anticipates on the ground that he discloses treatment of reversible obstructive airways disease	Amendment of 6/29/89 submitted, but not entered into the application. Amendment argued that all claims require (1) aqueous solution and (2) specific active ingredient. No single reference (Cairns,

				Dicker or Cox) discloses both.
7 4/3/89	'520 04/03/89	§103	Claims 1-17 rejected as obvious from Cox on the ground that Cox renders obvious the treatment of reversible obstructive airways disease	Amendment of 6/29/89 includes declaration of unexpected results submitted. Amendment not entered into the application.
8 3/8/90	'020 09/20/89	§102 (b), (e)	Claims 1-14 and 17 rejected as anticipated by Cairns and Dicker on ground of treatment of asthma, colitis and reversible obstructive airways afflictions.	Amendment of 9/12/90 (PTO Stamp date) further amends claim 1 to delete the eye, nasal and colon diseases and to limit the administration to the disodium salt of the active ingredient. Amendment made to more clearly focus the patentability issues related to the rejection and treatment of reversible obstructive airways disease. Other claims, not relevant here, also amended. None of Cairns, Dicker or

				Cox disclose use of aqueous solutions of nedocromil sodium for treatment of any disease.
9 3/8/90	'020 09/20/89	§103	Claims 1-14 and 17 rejected as obvious over Cairns and Dicker on ground to teaching of treatment of asthma, colitis and reversible obstructive airways disease obvious	See above. Plus, any *prima facie* obviousness is overcome by declarations establishing unexpected results.
10 3/8/90	'020 03/08/90	§102 (b)	Claims 1-17 rejected as anticipated by Cox.	See above
11 3/8/90	'020 09/20/89	§103	Cox renders obvious the treatment of reversible obstructive airways disease	See above
12 3/8/90	'020 09/20/89	§103	Claims 1-17 rejected as obvious over Fisons Japanese '722 on the ground that the publication teaches the claimed compound in an eye treatment and appears to anticipate the present claims.	Original claim 1 is amended, as stated above. Fisons '722 limited to treatment of eye diseases associated with diabetes and thus would not suggest the method now claimed to one skilled in the art. [Note: (1) No eye disease in original claim 1

				associated with diabetes; (2) The active ingredient in Fisons '722 appears to be a different compound than in the rejected claim 1 as amended.
13 12/10/90	'020 9/20/89	§102 (b), (e)	Claims 1, 7, 9-12 and 17 rejected as anticipated by Cairns and Dicker on ground of treatment of asthma, colitis and reversible obstructive airways disease	Proposed amendment of 6/12/91 (PTO Stamp date) cancels original claim 1 and replaces it with new proposed first claim 18. Proposed amendment is not entered into the application. [Proposed first claim 18 reintroduces the 6 types of eye diseases, the 3 types of nasal diseases, the reversible obstructive airways disease and the 3 types of colon diseases. Proposed first claim 18 also limits

				administration to soft, carbon dioxide permeable, plastics ampoule, sterile filled with unit dose of aqueous solution of active ingredient having pH 3.5 to 6.0. None of Carins, Dicker, Cox or Fisons '722 has "soft plastic ampoule."] Argument now shifts to patentability based on the soft plastic ampoule. Rule 116 amendment not entered. Preliminary amendment changes "soft ampoule" to – container--.
14 12/10/90	'020 9/20/89	§103	Claims 1, 7, 9-12 and 15-17 rejected as obvious over Cairns and Dicker re treatment of asthma, colitis and reversible obstructive airways disease obvious	See above.

15 12/10/90	'020 9/20/89	§102 (b)	Claims 1, 7, 9-12 and 15-17 rejected as anticipated by Cox on ground of treatment of reversible obstructive airways disease	See above.
16 12/10/90	'020 9/20/89	§103	Claims 1, 7, 9-12 and 15-17 rejected as obvious under Cox disclosure of treatment of reversible obstructive airways disease	See above.
Note: 12/10/90	'020 9/20/89		Claims 7, 9-12 and 17 rejected under 102 and 103 as unpatentable over Fizons '722	Not applicable to the recapture estoppel issue, because these claims are not directed to a method of treatment of eye disease. [They are directed to compositions.]
17 12/10/90	'020 9/20/89	§103	Claims 1, 7, 9-12 and 15-17 rejected as obvious over Cox, Cairns or Dicker in view of Cairns '85 publication or Auty render treatment of reversible obstructive airways disease	See above.
Note: Two claim 18's were				Preliminary amendment includes second

submitted; only the second claim 18 was entered into the application.				proposed claim 18, which differs from first proposed claim 18 in that it recites the contents of a "container" rather than a "soft ampoule;" does not recite it to be "sterile-filled" and includes the acid and pharmaceutically acceptable salt forms of the active ingredient.
18 4/8/92	'574 8/7/91	§112, ¶2	Claims 7, 10 and 17-22 are rejected on ground that the term "container" is indefinite, and the term "sterile-filled" is indefinite.	In an amendment dated 10/13/92 (PTO Date Stamp), claim 18 was amended to substitute -- ampoule—for "container"
19 4/8/92	'574 8/7/91	§103	Claims 7, 10 and 17-22 were rejected as obvious over Brown in view of Cox & GB # 291, on the ground that Brown teaches nedocromil sodium for inhalation; Brown teaches Crohn's & reversible airway obstructions; GB # 291 teaches reversible	In an amendment dated 10/13/92 (PTO Date Stamp) argument was presented that (1) GB #291 is equivalent to Brown; (2) Brown has pH of 5.0 to 7.5; (3) Brown does not teach an aqueous solution;

			obstructive disease; and Cox teaches reversible obstructive airways disease, and hard/soft capsules.	rather he discloses a process of making solid nedocromil sodium that is not even a pharmaceutical; (4) Examiner got concentration wrong: 33% - 17%; not 0.1-5; (5) Cox does not teach nedocromil; rather he teaches pyranoquinoline (closely related, but different compound) and thus Cox teaches away; (6) Cox teaches soft capsules to be swallowed; not plastic ampoule as claimed.
20 11/10/92	'574 8/7/91	§103	Final rejection of claims 7, 10 and 17-22 as obvious under Brown in view of Cox and GB # 291 Brown not equivalent to GB # 291; GB #291 has the claimed pH range of 3.5 to 6.0. Treats reversible obstructive conditions of the airway. Cox directed	In a proposed amendment dated 5/12/93 (PTO Date Stamp), it was proposed that in claim 18, line 10 after "aqueous," – pharmaceutical— was to be inserted. Arguments were made to the effect that the Examiner

			to Crohn's and reversible airway obstruction	is wrong re Brown; both teach pH 5.0-7.5; not 3.5 top 6.0. Brown has aerosol propellant; not aqueous solution. More argument re capsule, aqueous solution and what is/is not pharmaceutical. This amendment was not entered into the '574 application; but was entered as a preliminary amendment in the next application (the '804 application, below).
21 1/5/94	'804 6/25/93	§103	Claims 7, 10 and 17-22 were rejected as obvious over Brown v Cox & GB #291. Cox teaches active ingredient and method of treatment of reversible obstructive airways disease (18:64-65) and Crohn's disease (19:59).	In a "Response" dated July 5, 1994 (Applicant mailing date) no amendment to any claim was made. Rather, more argument was presented, with a good summary of issues and teachings of references.

22 10/19/94	'804 10/19/94	§103	Final rejection of claims 7, 10 and 17-22 as obvious over Brown v Cox & GB #291. Examiner alleges that Cox teaches active ingredient and method of treatment of reversible obstructive airways disease (18:64-65) and Crohn's disease (19:59). GB #291 pH reads on claim [Note: examiner states test backwards]. All art "reads on composition for treatment of reversible obstructive condition of the airways" and Crohn's.	In an amendment after final rejection date February 13, 1995 (Applicant mailing date), new attorney Napoli cancels claims 7, 10, 17-22. Adds new claims 23-25. Broadest method claim is new method claim 23, directed to method of treating a reversible obstructive airways disease comprising . . .. Amendment made "to present the rejected claim in a better form for allowance or appeal. Applicants continue to believe that amendments and reasoning set forth on 7/11/94 were sufficient to overcome the rejection under §103. Presents good argument why claims are patentable. Cox – only for oral or

				rectal administration; not inhalant
3/16/95	'804 6/25/93		Notice of allowance	Claims 23, 24 and 25 renumbered to 1, 2 and 3.